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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/326,106 | 06/04/1999 | GULILAT GEBEYEHU | 45-93A | 3765 |

23713 7590 03/09/2004

GREENLEE WINNER AND SULLIVAN P C
5370 MANHATTAN CIRCLE
SUITE 201
BOULDER, CO 80303

EXAMINER

MARSCHER, ARDIN H

| | |
|----------|--------------|
| ART UNIT | PAPER NUMBER |
|----------|--------------|

1631

DATE MAILED: 03/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

8/14

Office Action Summary

Application No.

09/326,106

Applicant(s)

GEBEYEHU ET AL.

Examiner

Ardin Marschel

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 September 2003 and 11 December 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 105-161 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 105, 106, 108, 109, 113, 114, 122, 124-137, 151, 152, 154 and 161 is/are rejected.
- 7) ☒ Claim(s) 107, 110-112, 115-121, 123, 138-150, 153, and 155-160 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Copy Not Made (Saheta) | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submissions, filed on 9/2/03 and 12/11/03, have been entered.

Applicants' arguments, filed 9/2/03 and 12/11/03, have been fully considered and they are deemed to be persuasive regarding previous rejections of record. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. However, upon reconsideration, the following rejections and/or objections are newly applied. They constitute the complete set presently being applied to the instant application.

PRIORITY CLAIM

If applicant desires priority under 35 U.S.C. 120 based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. It is noted that this appears as the first sentence of the specification following the title. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. ____" should follow the filing

date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

VAGUENESS AND INDEFINITENESS

Claims 124-137 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language. This claim is an omnibus type claim.

Claim 124, line 2, depicts the formula for the claimed polyamino acid with the A groups therein being both "A₁". This contrasts with the A group descriptions in lines 8 et seq. wherein the A groups have subscripts both of "1" and "2". It is unclear whether applicants wish to limit the claimed polyamino acid to the structural formula where the same A group, being "A₁" is meant for all embodiments or whether different A groups may be independently selected as in lines 8 et seq. of claim 124. Claims which depend directly or indirectly from claim 124 also contain this unclarity due to their dependence. Clarification via clearer claim wording is requested.

PRODUCT OF NATURE SUBJECT MATTER

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 105, 106, 108, 109, 113, 114, 122, 151, 152, 154, and 161 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter, which includes products of nature.

It is noted that the claims have been amended so that a polyamino acid is claimed which is reasonably interpreted as a chain of amino acid which contain (Z)

Art Unit: 1631

residues, linked by peptide bonds, commonly known as a polypeptide, with at least one R group attached thereto. Claims 105 and 161 also require that $m = 0$ also at least once in the claimed compound. It is noted that the claims are directed to a polyamino acid without any requirement such as isolated or purified to require the hand of man involvement in their obtaining or preparation, thus being inclusive of polypeptides of the claimed structure as are found in nature. The structural requirements, as explained below, of the claimed polypeptides are met by one or more polypeptides as found in nature and thus are products of nature which is non-statutory subject matter.

The structural requirements of the claimed polypeptides include five elements.

1) 2 – 2000 Z type amino acids (basic amino acids in claim 105 and generic amino acids as in claim 161) which are linked by peptide bonds, such as the peptide bonds in a polypeptide which is found in nature

2) parameter $m = 1$ at least once in the claimed compounds and at least 0 once in the claimed compound which defines the R group(s) attached to some Z amino acids

3) moiety R which is either a C_{1-23} alkyl or alkenyl or a steroid as listed in the claims.

4) termini of the compound are NH_2 and a carboxyl (claim 105) or, and a OH (claim 161) – It is noted that carboxyl end groups are commonly interpreted as $COOH$ thus also being inclusive of OH terminus practice. Such termini are commonly present in polypeptides found in nature

5) Open claim wording in the first line of each claim via the word “with” in the phrase “with the structure”. There is no definition of “with” in the instant disclosure as filed and a reasonable interpretation is thus taken as set forth on page 1324 of the New Riverside

University Dictionary as being open claim wording since the first three definitions in said Dictionary are "1. As a companion of"; "2. Next to"; and "3. Having as a ... characteristic". Having is also commonly understood in Patent claims to be an open claim language limitation. Therefore, the above listed claims are interpreted as including polypeptides which meet the above structural limitations via moieties or subparts thereof but may also contain other amino acids etc. corresponding to the open claim wording.

Claim 105 requires that the Z moieties be basic amino acids whereas claim 161 is more generic due to requiring that Z be amino acids without the "basic" limitation of claim 105. Thus, a product of nature which contains 2 or more basic amino acids with the appropriate R content as required above as well as the other structural limitation summarized above would be included both in instant claims 105 and 161 as embodiments. The basic amino acids are listed in Lehninger on page 71 as Lysine, Arginine, and Histidine. Chang et al. is also cited herein due to its descriptions of various amino acids of the methylated type. On page 469, first column, amino acids for comparative analysis are listed, such as Lysine, arginine, histidine, methylhistidine types, a monomethylarginine, a dimethylarginine types, a dimethyllysine type, and a trimethyllysine type of amino acid.

Christensen et al. discloses the primary sequence structure of portions of several methylated proteins which thus are natural products or non-statutory subject matter under 35 U.S.C. § 101. These proteins are polypeptide proteins thus containing peptide bonds and amino (NH₂) and carboxyl (or OH) termini but also specifically are cited in

Art Unit: 1631

Christensen et al. as containing the distinctive alkyl (methyl C_1) containing arginine (basic amino acid) residues. In particular Fibrillarin is disclosed in the reference wherein a segment is shown on page 1280 in Figure 1 which contains the basic dimethylarginine residue(s), as R with asterisk "*" at positions 8, 15, 21, 24, 28, and 31. Unmethylated Lysine (K) basic amino acid is shown at position 2 in Fibrillarin. At the top of page 1280, lines 1-5, fibrillarin is disclosed as a rat liver cell protein which is interpreted as being a natural product in rat livers. Therefore, the product of nature, fibrillarin contains 7 basic amino acid residues corresponding to $n = 7$ in the instant claims wherein the dimethylarginine is a methylated version of a monomethylarginine basic amino acid thus disclosing the $m = 1$ with $R = \text{methyl}$, a C_1 alkyl option for R in the instant claims. It is noted that there is no instant claim limitation that requires that the Z moieties in the claimed polyamino acid be contiguous to each other. The presence of unmethylated lysine denoted as K in the sequence of the reference is a disclosure of the $m = 0$ basic amino acid group as also required in the instant claims. Therefore, in summary the product of nature, that is, fibrillarin, is encompassed as an embodiment of the above listed instant claims thus supporting this rejection that the above listed claims are directed to include a product of nature which is non-statutory subject matter. Instant claims 113 and 114 are included hereinunder due to fibrillarin being a natural content of rat liver cells as well as nucleic acid and lipid aggregates, in membranes, thus making the compositions of claims 113 and 114 also encompass a product of nature. The kit claims 122 may only contain the claim 105 polyamino acid due to said claim 122 lacking any other specific limiting contents thus also included as being rejected hereinunder.

Additionally, in the more generic instant claim 161 the amino acid corresponding to Z is not limited to being basic in character. Consideration of the amino acids depicted in Lehninger on pages 69 and 70, it is seen that Threonine is a methylated version of Serine and Alanine is a methylated version of Glycine. Isoleucine is a methylated version of Valine. Therefore, with the instant claim limitations in claim 161 wherein $m = 1$ at least once in a common polypeptide and $m = 0$ at least once, any polypeptide which has a combination of residues of Threonine with Serine, or, Alanine with Glycine, or, Isoleucine with Valine meets the structural requirements of instant claim 161. On page 99 of Lehninger the natural protein, Human adrenocorticotrophin is disclosed in the lefthand column as well as Bovine ribonuclease. The Human adrenocorticotrophin contains both Alanine and Glycine and thus is encompassed within instant claim 161. Bovine ribonuclease contains Threonine, Serine, Alanine, Glycine, Isoleucine, and Valine and thus is also encompassed by instant claim 161. Thus, instant claim 161 additionally is properly rejected as containing products of nature which are nonstatutory subject matter under 35 U.S.C. § 101. It is also noted that contiguous amino acid residues are present in Bovine ribonuclease as cited above in that Thr and Ser is present as contiguous residues 15-18 and 77-78 thus making a potential contiguous Z moiety limitation in the instant claims ineffectual in overcoming this rejection.

Instant claim 108 is directed to a polysaccharide which also is claimed without any hand of man limitations. The structure contains n monosaccharide units optionally with or with an R moiety depending on the parameter m. It is noted that m may be zero for all monosaccharides in the claimed polysaccharide. In this case a glycosidically

Art Unit: 1631

bonded polysaccharide made up of common naturally occurring monosaccharides are encompassed by the claims. In Lehninger on page 227 Maltose, Lactose, and Sucrose, all products of nature are encompassed by the $m = 0$ embodiments of the instant claims with $n = 2$. In Lehninger at the bottom of page 228 starch in the form of α -Amylose is disclosed as consisting of long unbranched chains as depicted on page 229 at the top left of the page as a helical coil. This is encompassed in the instant claims with $n =$ a few thousand, deemed inclusive of 2000) as cited on page 229, first line, which is also a product of nature. In the case where $m = 1$ the mucopeptide shown on page 233 is encompassed by instant claim 108 wherein the R of the instant claims is an alkyl of 20 atoms in the peptide side chain of the mucopeptide. It is an alkyl due to containing alkyl moieties in the Alanine side chains thereof. It is noted that instant claim 108 lacks any limitation that limits the alkyl to distinguish over an alkyl containing peptide as in the mucopeptide of said page 233. The side chain of said mucopeptide includes cationic substituents as amino groups thus also including instant claim 109. The mucopeptide is contained in a cell which also contains nucleic acid or lipid aggregates in the cell wall as required in claims 151 and 152, respectively, thus also verifying these combinations as products of nature. The kit of claim 154 is included as it may only contain the polysaccharide of claim 108 due to no specific other requirement(s). Thus, non-statutory subject matter is encompassed by instant claim 108.

PRIOR ART

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

Art Unit: 1631

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 105, 106, 113, 114, 122, and 161 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Christensen et al. [BBRC 155(3):1278 (1988)].

Christensen et al. has been explained above as disclosing polyamino acids which are encompassed by the instant claims thus resulting in this disclosure also supporting the anticipation of the listed instant claims.

Claim 161 is rejected under 35 U.S.C. 102(b) as being clearly anticipated by Lehninger [BIOCHEMISTRY (1970)].

Lehninger has been explained above as disclosing polyamino acids which are encompassed by the instant claims thus resulting in this disclosure also supporting the anticipation of the listed instant claim.

Claims 108, 109, 151, 152, and 154 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Lehninger [BIOCHEMISTRY (1970)].

Lehninger has been explained above as disclosing polysaccharides which are encompassed by the instant claims thus resulting in this disclosure also supporting the anticipation of the listed instant claims.

INFORMATION DISCLOSURE STATEMENT

The following patent applications were cited in the Information Disclosure Statement, filed 9/2/03, for consideration: U.S. Patent application serial numbers: 08/450,555; 09/438,365; 09/937,837; 10/200,879; and 10/269,522. These are hereby acknowledged as having been considered. Consideration of 10/269,522 revealed that

Art Unit: 1631

this may contain a typographical error because it is directed to unrelated subject matter.

It was found, however, that 10/629,522 is a related application and is hereby also acknowledged as having been considered.

INFORMALITIES

The disclosure is objected to because of the following informalities:

Claim 112 contains the apparently misspelled word "diethylamioethyl".

Claims 138-150 are objected to due to containing the misspelled word "monosaccharrides" in the last line of claim 138.

Appropriate correction is required.

CLAIM OBJECTIONS

Claims 107, 110, 111, 115-121, 123, 153, and 155-160 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the Central PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center number is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (571) 272-0718. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (571) 272-0722.

Art Unit: 1631

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Tina Plunkett, whose telephone number is (571) 272-0549.

March 5, 2004

A handwritten signature in black ink, appearing to read "Ardin H. Marschel".

ARDIN H. MARSCHEL
PRIMARY EXAMINER